REMARKS

In view of the above amendments and the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow Claims 1 to 10 and 12 to 26, as well as newly added Claims 27 to 49, the only claims pending and under examination in this application.

Claim 1 has been amended to clarify the language of claim 1, support for this amendment being found, e.g., at page 8, first complete paragraph. Certain of the claims have been amended to remove multiple dependencies. In addition, original claim 11 has been deleted and new claims 27 to 49 have been added. The new (independent) claim 27 is based on a combination of original claims 1 and 11 and new claims 28 to 36 are dependent on this new independent claim. The new (independent) claim 37 is based on a combination of original claims 1, 11, 12 and 13 and new claims 38 to 45 are dependent on this claim. The new claims 46 to 49 correspond to original claims 17 to 19 but refer to the methods of claims 27 and 37. As the above amendments introduce no new matter, their entry by the Examiner is respectfully requested.

Claims 1 to 6 have been rejected under 35 U.S.C. § 112, second paragraph, for certain phraseology appearing in claims 1 and 4. In view of the above amendments to claims 1 and 4, this rejection may be withdrawn.

The Examiner has next rejected original claims 1-3, 5, 6, 20 and 22 as being unpatentable 35 U.S.C. § 103(a) over Roser I (US 5,149,653) in view of Illum et al (US 6,391,318) and Chatfield (US 6,136,606) and in view of Roser PCT (WO 96/40077) and Roser II (US 6,221,575).

The present invention, as is claimed in claim 1, is a method of preserving biologically-active material. The claimed method comprises a first step wherein an aqueous suspension of the biologically-active material is mixed with an aqueous solution of chitosan (or non-toxic salt thereof) so as to form a coacervate. The coacervate, as explained in the specification at page 6, lines 24-27, is an absorption complex of the chitosan and the biologically-active material wherein the biologically-active material is coated with the chitosan to form a protective "shell" around the biologically-active material (specification,

page 6, lines 6-8). Following the formation of the coacervate, it is then mixed with the trehalose solution. The mixture obtained is then subjected to drying at a pressure less than atmospheric and at a temperature which is initially less than or equal to 37°C and which temperature is prevented from falling to 0°C or below to form a glassy trehalose matrix containing, within the matrix, desiccated biologically-active material and chitosan (or non-toxic salt thereof).

Roser I discloses a method for preserving of viruses using trehalose. According to Roser I (column 2, lines 1-3), the presence of trehalose in the viral medium during drying either frozen or at ambient temperature enables live viruses to be preserved. The method of Roser I comprises mixing an aqueous system containing the virus with trehalose. Roser I neither teaches nor suggests making a coacervate of the virus and chitosan and then mixing the coacervate with trehalose. When, according to Roser I, a mixture of the aqueous system containing the virus and trehalose is prepared, this mixture is then subjected to freeze drying or to drying at ambient temperature. Roser I, in subjecting the aqueous virus/trehalose mixture to freeze drying, is not taking care to prevent the temperature from falling to 0°C or below. Roser I does not teach or suggest the drying procedure according to the present invention whereby drying is carried out at a pressure below atmospheric and at a temperature which is initially less than or equal to 37°C and which may fall provided that the temperature does not fall to, or below, 0°C. Roser I, also, does not produce, according to the method used, a glassy porous matrix comprising metastable glassy trehalose containing, within the matrix, desiccated biologically-active material and chitosan.

Both Illum and Chatfield describe vaccine compositions which contain chitosan. Illum discloses a vaccine composition adapted for intranasal administration which comprises an antigen and an effective adjuvant amount of chitosan (or non-toxic salt). The vaccine composition is prepared for use, according to Illum, by mixing a solution of the antigen with a solution of the chitosan to give the required concentrations. It appears that the invention of Illum is based on their discovery that, upon intranasal co-administration, chitosan enhances the immune response of antigens and thus provides an adjuvant effect (Illum, column 2, lines 41-43).

It is clear that any combination of the teachings of Illum and Roser I would not result in the invention claimed in the present application. Should a person skilled in the art wish to combine the teachings of these documents, he/she would take the aqueous system containing the virus and trehalose (as taught by Roser I) and add chitosan to this prior to freeze drying or prior to drying at ambient temperature (according to Roser I) to obtain a freeze dried or an ambient temperature dried mixture of trehalose, virus and chitosan. In no case would the skilled person (according to the teaching of Roser I or Illum) make a coacervate of the virus and chitosan, then mix this with trehalose and then subject the coacervate/trehalose mixture to drying at a pressure less than atmospheric and at a temperature which is initially less than or equal to 37°C and which may thereafter fall provided that the temperature does not fall to, or below, 0°C. The product that may be obtained by combining the teachings of Roser I and Illum will not be a glassy porous matrix comprising metastable glassy trehalose containing, within the matrix, desiccated-active material and chitosan.

Chatfield also discloses a vaccine composition comprising a mixture of an antigen and a chitosan solution, the chitosan being included into the composition to provide an adjuvant effect. Combination of the teachings of Roser I and Chatfield could not (for reasons given above in respect of Illum) result in the method claimed in claim 1 of the present application.

As is stated in the specification for the present application (page 6, lines 6-10), the use of chitosan in the present invention is based on the discovery that it acts as a protective biopolymer shell around the biologically-active material being preserved. Thus, the use of chitosan in combination with the controlled method of desiccation gives an improved thermal tolerance to the desiccated material. This is a technical effect upon which the present invention is based. This technical effect is not disclosed in Roser I and is not disclosed in either Illum or in Chatfield. The technical effect arising in respect of the use of chitosan in Illum and in Chatfield is derived from the adjuvant effect of chitosan. There is, thus, no reason to be derived from Illum or from Chatfield why chitosan should be employed in the way it is employed in the present invention.

The Examiner also cites Roser PCT and Roser II since he acknowledges that Roser

I does not teach that viral compositions can be dried, using trehalose, using vacuum drying techniques.

Roser PCT teaches the production of foamed glass matrices using trehalose, which matrices may include a bioactive substance. However, as mentioned above in connection with Illum and with Chatfield, there is no suggestion in Roser PCT that any improved thermal tolerance could be provided to a biologically-active material by incorporating chitosan in the way that it is incorporated in the method of the present invention. Cleary, on the basis of the teaching in Illum or in Chatfield, a skilled person would not be directed towards incorporating chitoan in a foam glass matrix of Roser PCT by firstly forming a chitosan-biologically-active material coacervate prior to admixture with trehalose before the vacuum drying stage.

Roser II does not add to the disclosure of Roser PCT.

For the reasons provided above, claims 1-3, 5, 6, 20 and 22 are not obvious under 35 U.S.C. § 103(a) over Roser I (US 5,149,653) in view of Illum et al (US 6,391,318) and Chatfield (US 6,136,606) and in view of Roser PCT (WO 96/40077) and Roser II (US 6,221,575) and this rejection may be withdrawn.

Finally, Claim 4 has bee rejected under 35 U.S.C. § 103(a) as obvious over Roser I (US 5,149,653) in view of Illum et al (US 6,391,318) and Chatfield (US 6,136,606) and in view of Roser PCT (WO 96/40077) and Roser II (US 6,221,575); and further in view of Rweyemamu et al and Gombotz et al (US 5,900,238). In view of the fundamental deficiency in the primary five references as discussed above, and the fact the final two references cannot make up this fundamental deficiency, this rejection may be withdrawn.

CONCLUSION

In view of the above amendments and remarks, this application is condidered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issue.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number STHP-002.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: 9.18.03

By: _____
Bret E. Field
Registration No. 37,620

BOZICEVIC, FIELD & FRANCIS LLP
200 Middlefield Road, Suite 200
Menlo Park, CA 94025
Telephone: (650) 327-3400
Facsimile: (650) 327-3231
F:\document\sthP\002\response to 3-25-03 office action.doc